UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,098	03/22/2000	MASAYUKI TSUCHIYA	053466/0274	7563

22428 7590 11/09/2004

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
HELMS, LARRY RONALD	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,098	TSUCHIYA, MASAYUKI	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-23* is/are pending in the application.

4a) Of the above claim(s) *6-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/23/04 has been entered.

2. Claims 6-23 are pending. Claims 15-23 have been added and claim 14 has been amended.

3. Claims 6-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

4. Claims 14-23 are under examination.

5. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

6. The following Office Action contains NEW GROUNDS of rejections.

Rejections Withdrawn

7. The rejection of claim 14 and claims 3-5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

8. The rejection of claims 3-5 and claim 14 under 35 U.S.C. 103(a) as being unpatentable over Sato et al (Molecular Immunology 31:371-381, 1994, IDS #4) and further in view of Queen et al (PNAS 86:10029-10033, 1989, IDS #4) is withdrawn in view of the amendments to the claims.

9. The rejection of claims 3-5 and claim 14 under 35 U.S.C. 103(a) as being unpatentable over Co et al (PNAS 88:2869-2873, 1991, IDS #4) and further in view of Queen et al (PNAS 86:10029-10033, 1989, IDS #4) is withdrawn in view of the amendments to the claims.

10. The rejection of claims 3-5, and 14 under 35 U.S.C. 103(a) as being unpatentable over Roguska et al (Protein Engineering 9:895-904, 1996, IDS #3) and further in view of Queen et al (PNAS 86:10029-10033, 1989, IDS #4) is withdrawn in view of the amendments to the claims.

The following are NEW GROUNDS of rejections

Claim Rejections - 35 USC § 112

11. Claims 14-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 14-23 are indefinite for reciting "high homology" in claim 14 because it is not clear what the phrase means. Does the phrase mean 70%, 80%, 90%, 99%?

b. Claims 14-23 are indefinite for reciting part (4) in claim 14 because it is unclear if the method is replacing a FR1 with a FR2 that is human or replacing one FR with the corresponding FR from a human.

c. Claim 17 is indefinite because it is unclear what the searched sequence is and what the target sequences is in claim 14. Claim 14 does not recite any target sequence.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 14-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing a humanized antibody by the method of claim 14 wherein the final antibody recovered from the culture binds antigen that is the same as the antibody from the first animal species and the humanized antibody comprised all six CDRs from the first animal species, does not reasonably provide enablement for a method of producing a humanized antibody wherein the antibody does not bind the same antigen or does not comprise six CDRs from the first animal species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They

include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to an antibody that only has one CDR from the first animal species and any other CDRs from any source and the antibody does have to bind the same antigen as the antibody of the first species or FR replaced that are not corresponding FR (i.e. FR1 replaced with FR2). The specification teaches that the humanized antibody for HM1.24 binds the same antigen as the "primary design" antibody and has the six CDRs from the mouse antibody (see Example 1 pages 71-81). The specification does not enable the claims as broadly recited.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable

regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that humanized antibodies as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions in unspecified order have the required binding function. The specification provides no direction or guidance regarding how to produce antibodies as broadly defined by the claims. Undue experimentation would be required to produce the invention commensurate with the scope of the claims from the written disclosure alone.

Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention.

14. Claims 20-21 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claims 20 and 21 recite "is from one to ten". The response filed 7/23/04 states that support for the limitations can be found at page 15, lines 1-4 in the specification. The specification recites at this location "a plurality of amino acid residues mean 2 or more amino acid residues, preferably 2 or more and 10 or less amino acid residues". In this context the specification teaches 2 or more or 10 or less but does not recite "one to ten". It only contemplates 2 to 10 or 2 up to 10. There is no support for "one to 10" amino acids being substituted. Applicants are required to provide specific support for the limitation in the specification as originally filed or remove it from the claims.

15. Claims 14-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Newly added claim 14 recites step (4) part i). The response filed 7/23/04 states that support for the limitations can be found at page 74, lines 2-30 and page 11, lines 8-28. The specification does not recite support for selecting a FR that has "at corresponding positions the same amino acid residues as the amino acid residues introduced by the substitution in step (1)". The specification at the recited locations disclose choosing a homologous FR but the specification does not disclose picking the FR so that the amino acids that were replaced or substituted in part (1) are retained.

There appears to be no support for choosing a human FR that retains the substituted residues. Applicants are required to provide specific support for the limitation in the specification as originally filed or remove it from the claims.

16. Claims 14-23 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 14-23 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed 7/23/04. In that paper, applicant has stated "In fact, the homology search is carried out on all 8 FRs (including FRs in which amino acid has not been substituted) in the H chain and L chain." (see page 7 of response), and this statement indicates that the invention is different from what is defined in the claim(s) because in claim 14 the homology search is only directed to the amino acid sequence of the FR in step (1) wherein residues have been substituted. Thus, there is no homology search over all 8 FRs as stated in the response.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30

am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Larry R. Helms

571-272-0832